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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/281,674	03/30/1999	HERMANN BUJARD	BBI-013C3CN2CPA	7512

959 7590 05/21/2002

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	18

DATE MAILED: 05/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/281,674	Applicant(s) BUJARD ET AL.	
	Examiner Ram Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-14 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-14 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

1. The response filed 3-8-02 has been entered.

2. Claims 1-6, 9-14, 17-19 are under consideration in the instant application.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claim 1-6, 9-14, and 17-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. U.S. Patent No. 5,888,981, for reasons of record set forth in the previous office action of 5-23-00. Although the conflicting claims are not identical, they are not patentably distinct from each other because the invention of the instant application cannot be practiced without infringing on the invention of the cited patent.

Applicants have stated that a Terminal Disclaimed in compliance with 37 CFR 1.321(c) would be submitted when the claims are otherwise indicated allowable.

5. Claims 1-6 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of regulating expression of a tet operator-linked gene in a cell, wherein a first nucleic acid molecule comprises the

molecule comprises the tet-operator linked gene whereas a second nucleic acid nucleic acid encodes a tetracycline-controllable transactivator tTA which comprises a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eukaryotic cells, wherein the method is carried out in a cell in vitro or in vivo wherein both the nucleic acids are administered directly to the cell, or an ex vivo method wherein both the nucleic acids are introduced in a cell and the cell is administered to a subject, does not reasonably provide enablement for the claimed wherein the cell is present in a subject in vivo and one or both the nucleic acids are administered by different methods or wherein cells have integrated one nucleic acid in the genome at a site or at randomly and the second nucleic acid is administered by any method or a method wherein the first nucleic acid is present in a cell, the cell is administered to a subject and the second nucleic acid is administered to the subject by any method or any other embodiment, for reasons of record set forth in the previous office action of 8-28-01. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 3-8-02 have been fully considered but they are not persuasive. In the pages 2-3 of the response applicants have listed as to how the specification provides guidance for the claimed invention. On page 4 applicants provides a list of 12 of references in support of their arguments that the method has been successfully used in many scientific publications. In pages 5-7 applicants again argue as to how there is sufficient disclosure for practicing in vivo methods and also list references in support of their argument. It is noted that the a scope of rejection was given in the previous office action and that the claimed method was enabled as it pertained to direct administration to a tissue in vivo or ex vivo method wherein both the nucleic acids are introduced in a cell that is to be administered to a subject. None of the articles that are cited by the applicants in their response or

the sections of the specification stated in the response provide any evidence that the method could be practiced when the nucleic acids were administered to a subject by any route in vivo or when the two nucleic acids were present in two different cells and the cells were administered to a subject. It is noted that in the previous office actions enablement issues were raised based on sound scientific reasoning and based on the state of the art at the time of the invention. Applicants have not addressed specific issues raised in the office action, rather they have made general statements and these statements are not sufficient to address the scientific issues raised in the previous office action. Furthermore, the references listed on page 6 deal with direct administration of the nucleic acids into the tissues, which support the position taken in the previous office action. Applicants on page 7, last but one paragraph state that their example 2 along with citations discussed provide enablement for in vivo method. However, it is noted that example 2 is a transgenic mouse and making of a transgenic mouse can not be compared to a method of in vivo gene delivery by any route. Applicants further add that scope of invention should not be limited based on potential difficulties of gene therapy and gene delivery or of examiner's anticipated failure of the procedure and that an skilled artisan would be able to practice the method. In response, it is noted that the state of the art as evidenced by reviews is what known to an artisan of skill and the specification of an application has to correct the deficiency of practicing the claimed invention recognized in the art. Applicants arguments that the specification does not have to teach examples of every different embodment encompassed by the claims, it is noted that the specification as filed has to enable the full scope of a claim.

It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991).

Furthermore, As set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving

predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In conclusion, the scope of the enablement rejection of claims 1-6 and 9 as set forth in the previous office action of 8-28-01 is maintained.

6. Claims 10-14, 17, and 19 are free of the prior art of record.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to **§** 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER